

Fatal ventricular fibrillation after treatment with digoxin in a 27-year-old man with mitral leaflet prolapse syndrome

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SUMMARY A 27-year-old man with typical mitral leaflet prolapse syndrome was under medical care for eight years with ventricular arrhythmias resistant to various antiarrhythmic drugs. He was started on digoxin, 0.25 mg daily, because of echocardiographically demonstrated left ventricular dilatation and functional impairment: he died of ventricular fibrillation 15 days later.

The prognosis of the mitral leaflet prolapse syndrome, which is among the commonest of cardiac abnormalities, is generally good,¹ though a few sudden deaths, probably caused by ventricular arrhythmias, have been reported.² We report a patient who was under observation for eight years and who died of ventricular fibrillation 15 days after starting treatment with digoxin.

Case report

A male engineer, previously under medical care for three years because of a systolic murmur and ventricular extrasystoles at rest, was admitted to hospital at the age of 23 after a syncopal episode. Initial electrocardiogram monitoring showed bigeminal ventricular extrasystoles, which did not respond to lignocaine infusion, beta-blocking agents, procainamide, or phenytoin. He was not dyspnoeic or febrile and there was no tachycardia, gallop rhythm, pericardial friction rub, or raised jugular venous pressure. Radiologically, slight cardiac enlargement was evident. The 12 lead electrocardiogram was normal apart from wide QRS ectopics. On subsequent treatment with propranolol 20 mg three times daily, the patient continued to experience palpitation and sensations of dizziness, but no further syncope. During the next three years quinidine alone or in combination with beta-blocking agents failed to abolish the extrasystoles, and eventually no further treatment was given.

At the age of 26 the patient was examined for the first time at Oulu University Centre. A mid-systolic click and late systolic murmur of mitral regurgita-

tion, both uninfluenced by postural manoeuvres, were heard over the cardiac apex. The resting 12 lead electrocardiogram showed negative T waves in leads III and aVF, and low QRS voltages in the standard leads. The chest x-ray film was normal. Echocardiography showed end-systolic mitral leaflet prolapse and a suspicion of thickening of the mitral leaflets (Fig. 1). The echocardiographic left ventricular end-diastolic diameter was 60 mm, and ejection fraction 73 per cent. Though the patient continued to experience palpitation, no treatment was given.

At a follow-up examination one year later the left ventricular end-diastolic dimension was 66 mm, and the ejection fraction 54 per cent. The resting 12 lead electrocardiogram showed low voltages, negative T waves in leads III and aVF, and U waves in leads I and aVL. The PQ and QTc intervals were normal. In view of the left ventricular dilatation and reduced ejection fraction noted in the echocardiogram, treatment was started with digoxin, 0.25 mg daily. Fifteen days later, while at home watching television, he suddenly lost consciousness and became pulseless. Resuscitative efforts, started by relatives, were continued in the hospital for three and half hours without success. Electrocardiographic monitoring upon admission showed ventricular fibrillation and this proved resistant to lignocaine, procainamide, and DC countershock.

At necropsy left ventricular hypertrophy was found, the myocardium measuring 2 cm at maximum thickness. The posterior leaflet of the mitral valve was thick, floppy, and bag-shaped. The other

valves were normal. The gross anatomy of the coronary arteries was normal and nothing suggesting myocardial infarction was noted. Histologically (Fig. 2), the mitral leaflet showed abundant deposition of material which was Alcian Blue positive, diastase resistant, and PAS positive, characteristic of myxomatous degeneration.

Discussion

"The prognosis of the patient with mitral leaflet prolapse syndrome largely depends on whether there is an underlying cause or associated condition."¹ Despite the high prevalence of arrhythmias in the syndrome, only a few sudden deaths, possibly caused by ventricular fibrillation, have been reported.^{2,3} The pathogenesis of the ventricular arrhythmias is not understood.⁴ There are suggestions that ventricular ectopy is independent of valve dysfunction and operates on the basis of a primary myocardial disorder.^{1,5} In the present case underlying or associated cardiomyopathy is perhaps

suggested by the finding of left ventricular wall thickening. On the other hand, ventricular arrhythmias could arise from stretching of the valve leaflet tissue with augmented myocardial pacemaker activity by a mechanical stimulus effect or by ischaemia from increased papillary muscle tension.⁶ These mechanisms could also alter ventricular refractory properties or conduction and possibly lead to ventricular re-entry.⁷ In some cases of mitral leaflet prolapse syndrome accessory conduction pathways exist as in the Wolff-Parkinson-White syndrome, even though there may not be any evidence on the surface electrocardiogram.^{8,9} Treatment of ventricular arrhythmias in symptomatic patients, particularly if the resting electrocardiogram shows inferoposterior ST segment and T wave changes,¹⁰ is recommended with beta-adrenergic blocking agents,¹¹ though these are not always effective.¹

Digitalis has been used previously,^{12,13} and there has been no claim that it had any connection with the fatal outcome in the reported cases of sudden death, though caution has been urged in respect of the use of this drug in these patients.⁹

The liability to arrhythmias caused by digitalis toxicity has been found to be increased in some cardiac diseases such as myocardial infarction and in certain cardiomyopathies.¹⁴ Arrhythmias produced by digitalis are the results of alterations in impulse formation or conduction or both.¹⁵ Ventricular ectopic activity is increased by bringing the phase IV resting potential closer to the threshold potential. In the mitral leaflet prolapse syndrome ventricular automatism could be further enhanced by alteration in pacemaker activity, caused by the inotropic action of digitalis with stretching of the papillary muscle. On the other hand, in view of the possibility of accessory conduction pathways,⁹ digitalis glycosides could be hazardous in certain re-entry phenomena by reducing the effective refractory period.^{7,8,16} In the present case, the relatives were unable to give any history suggestive of digitalis intoxication, and the serum digoxin concentration was not assayed. Moreover, no factors predisposing to electrolyte disturbances were apparent. Objective evidence of the Wolff-Parkinson-White syndrome and supraventricular arrhythmias is lacking, so that we cannot reach any conclusion concerning the mechanism of the fatal episode of ventricular fibrillation in our case. The timing of events does, however, suggest an association between digoxin treatment and the fatal event.

This case raises the possibility that starting treatment with digoxin in patients with mitral leaflet prolapse, abnormalities of the resting electro-

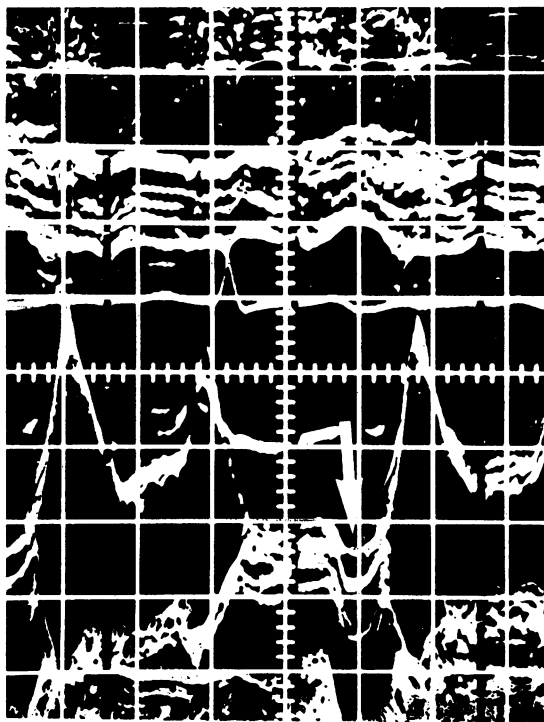


Fig. 1 M-mode echocardiogram from the mitral valve showing the late systolic mitral prolapse (arrow). Note also the slightly thickened posterior mitral leaflet (in diastole) indicating possible myxomatous infiltration.

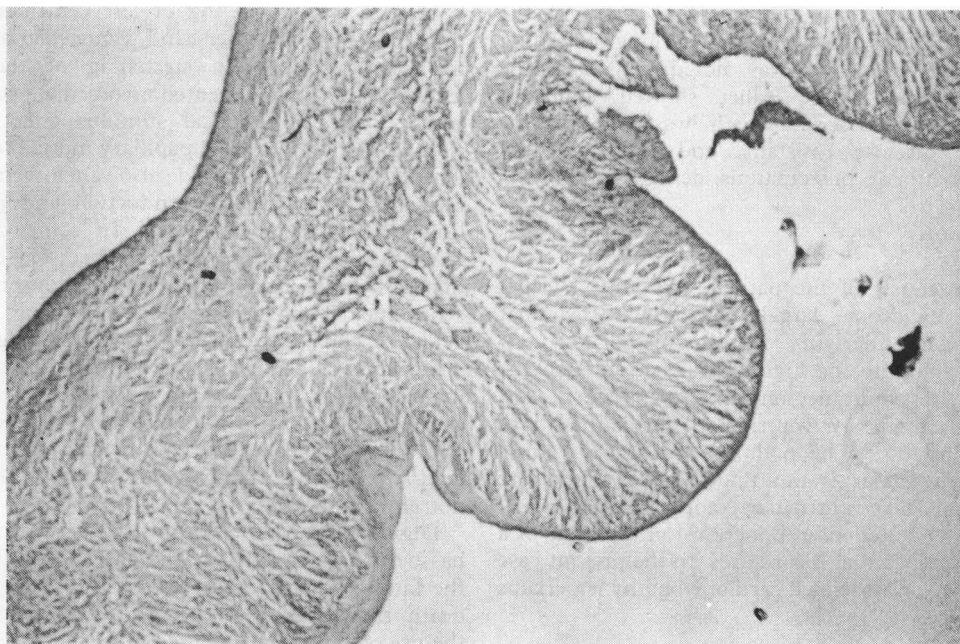


Fig. 2 This figure shows extensive deposition of myxomatous material within the fibres of the posterior leaflet of the mitral valve. The atrial surface is at top left. (Alcian Blue stain at pH 2.5. Original magnification $\times 33$.)

cardiogram, and ventricular ectopic activity may result in ventricular fibrillation. This possibility should be considered and it should be the subject of further study.

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